PHILADELPHIA NEUROLOGICAL SOCIETY.

October 25th, 1897.

The President, Dr. Charles W. Burr, in the chair.

Dr. A. Ferree Witmer exhibited

A CASE OF AKROMEGALY.

The patient was a female, aged fifty-five, unmarried, and a native of Ireland. The early personal and family history were negative. The time of onset of the disease was unknown. A photograph of the patient, taken in 1876, showed disproportionate development of the lower part of the face, including the pinna of the ear. The woman applied for treatment of a dull, intermittent pain in the left knee joint. The joints throughout the body were fully movable and non-crepitant. She complained also of somnolence so intense that she frequently fell asleep while at work. This condition had been noted for two years, and was as likely to occur in the morning as in the evening hours, and was increasing in degree. She had complained of vertigo for a period of six months, about two years ago, and had a dull morning headache also at that time. The tongue was swollen at times. The voice had become deeper in pitch, the speech slow and muffled, the appetite slightly in excess, and the thirst constant. The urine was voided frequently and in large quantities. She had intractable diarrhea at irregular intervals, and had had the menopause twelve years ago, and no abnormality had been noted throughout its course. She had hot and cold flushes; her extremities were always comfortably warm. She was not oversensitive to heat or cold; her memory had failed slightly; she had worn a number five boot comfortably five years ago, but a number seven was now required. There were no disturbances of the special senses.

The weight of the patient was two hundred pounds; her height was five feet six inches.

The enlargement was general and not circumscribed to the extremities. Skiographs of the hand and foot showed marked increase of the soft parts, possibly with changes in the cartilages, but with no increase of the bony structure. Fluoroscopic examination of the lower jaw and of the thorax showed proportionally no increased amount of bone. Her hair was abundant and natural in color; her skin was puffy and pitted slightly on pressure over the dorsum of the hands; the face was elongated but symmetrical; the eyelids were enlarged; the nose was thickened; the cheek bones were prominent; the cheeks were flattened; the lower lip was protruded; the tongue was large, flabby and slightly fissured; the palate was highly arched; the cartilages of the larynx and nose were hypertrophied; the lower jaw was very prominent; the neck was short and thick, and the thyroid body was not prominent. There was no retrosternal dulness; there was slight cervico-dorsal kyphosis. The measurements of the trunk and extremities gave normal averages in length, but the width was materially increased. The nails of the fingers and toes were normal in appearance; the heart and lungs were normal; the respiration was shallow; the urine was of low specific gravity, 1008 at one examination, but contained no albumin, no sugar, and no peptone; the eyeballs were slightly prominent; the visual fields for form and color were normal; the pupils responded freely to light in accommodation and in convergence, and a far-sighted astigmatism of mild degree was present. Tests to determine rate of sense perception gave high thresholds in every instance, showing an average retardation of reaction time to forty per cent. below the normal. Dynamometer tests indicated average strength. The knee jerks were sluggish; there was no clonus; the station was normal, and the gait was quick. The medication consisted of an extract of thyroid body in doses of fifteen grains daily for a period of three months, but this was without benefit—and later of eight grains of an extract of pituitary body daily for two months, which also was without apparent benefit.

Dr. Spiller exhibited, in the names of Drs. F. A. Packard and H. W. Cattell,

THE BRAIN AND SPINAL CORD FROM A CASE OF AKROMEGALY.

He stated that Strümpell had recently remarked on the great number of cases of akromegaly in which tumor of the pituitary body had been found.

The specimens presented were from a case which had been reported clinically by Dr. Packard. A large tumor which proved to be a round-cell sarcoma, and was about the size of an English walnut was found in the pituitary body, and had eaten away the base of the skull by pressure. The optic nerves were much pressed upon, and the nasal side of the right nerve was degenerated. The left had not, at that time, been examined. Large calcareous plates were found in the pia-arachnoid of the cord, and were very numerous. These were not supposed to have been in relation with the akromegaly.

The speaker stated that it is difficult to believe that a small gland, such as we know a part of the pituitary body to be, could by its altered functions produce the appearances of a systemic disease like akromegaly, though he could not deny the possibility of this. He said that occasionally the gland had been found diseased when the symptoms of akromegaly had not been present, as in a case reported by Dr. Packard in connection with this case of akromegaly. The frequency of disease of the pituitary body in cases of akromegaly, he thought, did not prove conclusively that this is the cause of the latter affection.

He stated that he had been much interested in the possibility of surgical interference in cases of akromegaly in which the symptoms rendered the diagnosis of a tumor of the pituitary body probable, as in this case, in which bilateral temporal hemianopsia, with optic atrophy, intense headache, somnolence, absence of the patellar reflex, and failure of memory, were present. In other cases in which the diagnosis of tumor could not be made, the question of operation, of course, would hardly arise. If we believe that altered function of the pituitary body is the cause of akromegaly, he thought that we might well dread the effects of removal of the entire gland. He regretted that

Dr. Keen had been unable to be present to discuss this important question, and read the following communication from him:

"You are at liberty to say that my experience in the case of brain tumor in the frontal lobe, operated on in Baltimore a year ago last spring with Dr. H. M. Thomas, and shown at the meeting of the American Neurological Association here not long afterward, would make me believe that by lifting an osteoplastic flap from the forehead, either in one large piece or possibly better by one flap, on each side, it would be possible to reach the pituitary body. Whether the hemorrhage and other emergencies that might then arise would be too difficult to cope with, I do not know, but I should believe that we could do so successfully."

DISCUSSION.

Dr. F. A. Packard:—I have nothing particular to add to what Dr. Spiller has said. The condition of the patient remained practically unaltered from 1892 until the last time I saw him, six months before his death. Between 1886 and 1896, there was no return of the attacks of somnolence. If the somnolence had been due to the tumor, is it presumable that it would have continued.

There was no loss of smell when I last tested it a year ago.

There was one sympton which was never sufficiently studied, because it was difficult to get hold of the man, and that was the profuse secretion from the nose. The patient had constant severe headache which brought tears to his eyes, and it was a question whether this secretion was not composed in great part of tears. On one occasion I found that this fluid contained a large quantity of sodium chloride, a good deal of nucleo-albumin, and under the microscope a large number of mucus corpuscles.

The fields of vision were tested a second time in 1894 or 1895 by Dr. de Schweinitz and found to be contracted in all directions, though previously there had been bitemporal hemianopsia. There was no material change from the report in 1892. I ascribed the increase in visual power to necrosis of the sella turcica allowing more room for the spreading out of the nerve fibres, although this explanation did not seem to be entirely satisfactory. It is possible that a hemorrage occurred in the tumor in 1885, giving rise to increase of bulk of the mass, and so producing somnolence and hemianopsia which ceased as the blood was absorbed.

Dr. Francis X. Dercum:—I am glad to see these interesting specimens as I saw the patient many times during life. I am also pleased to hear that Dr. Spiller takes the position that I did some years ago, namely, that it is not philosophical to ascribe the symptoms of akromegaly to disease of the pituitary body. As a matter of fact, there is scarcely a gland in the body that has not been described as enlarged in certain cases of this affection. It, therefore, seems premature to ascribe it to disease of the pituitary body, even if we exclude those cases in which this has been found to be normal.

Dr. A. A. Eshner:—I should like to say in connection with this subject that Woods Hutchison, in reporting a case of akromegaly, with enlargement of the pituitary body in a giantess (*American Journal of the Medical Sciences*, 1895, p. 190) suggests that at least one form of giantism is merely akromegaly beginning in fœtal or infantile life. He offers the further suggestion that the nutrition of the body may be presided over by structures in the pituitary region. A series of measurements showed that while the pituitary fossa in the skulls of cretins and dwarfs is markedly contracted in size, it is unusually enlarged in cases of giantism and akromegaly, as well as in the skulls of the anthropoid apes, which present some features of akromegaly.

In reference to the question of surgical interference, I would call attention to the fact that in the *British Medical Journal* for 1893 (No. 1722, p. 1421) Caton reported a case of akromegaly with symptoms of intracranial pressure. An opening was made in the skull with relief of suffering and prolongation of life. Operation had been recommended earlier but was not at first consented to. It was hoped that by opening the skull the intense pain could at once be relieved, and subsequently the enlarged pituitary body be removed. Accordingly the bones forming the anterior portion of the right temporal fossa were removed, but at no time did the condition of the patient appear suitable for the more radical operation. Upon post-mortem examination the pituitary body was found to be as large as a tangerine orange and presenting histologically the structure of a round-cell sarcoma. In commenting on this report at the time, I took occasion to say that "the unfortunate outcome of the case . . . lay in the nature of the case itself, rather than in a failure of the operation or of the principles on which it was based, . . . and in future the propriety of operation in selected cases of akromegaly should receive due consideration."—*(Medical News,* Jan. 27th, 1894, p. 108.)

Dr. A. Ferree Witmer:—In the case that I present, perverted sleep has been a marked symptom, but there probably is no tumor as the eye grounds are normal, there is no staggering gait, and the knee jerks are normal.

Dr. James Hendrie Lloyd reported

A CASE OF TOTAL AND COMPLETE UNILATERAL OPHTHALMOPLEGIA (BOTH EXTERNAL AND INTERNAL).

The patient, a man, aged thirty-eight years, had at first what appeared to be simply a paralysis of the third nerve of the right eye. Later, however, the fourth and sixth nerves also became involved. The eyeball was absolutely immobile and was directed forward. There was complete ptosis, and the pupil did not respond to light or on accommodation. Severe headache was felt, and this was located above and behind the orbit. Slight exophthalmos was noticed later. The sensory tests were of great interest there was complete anesthesia of the conjunctiva and in the whole territory of the supraorbital nerve as far back as the vertex. Both the upper and lower lid were anesthetic on their edges, except towards the inner canthus, and this indicated that the nasal branch of the ophthalmic nerve was not completely involved. This was shown also by the fact that the mucous membrane on the interior of the nostril and the small patch of skin on the nose supplied by this branch were not anesthetic. There was retardation of tactile sense, but not complete loss, in the territory of the superior maxillary nerve. The inferior maxillary division of the fifth was entirely exempt, as was also its motor branch. The seventh and eighth nerves were not involved. There was a slight choking of the disk of the affected eye. The diagnosis of a syphilitic lesion just behind the orbit was made. The autopsy revealed a gummatous inflammation behind and extending into the orbit. It had also invaded the walls of the cavernous sinus. The Gasserian ganglion was not included in the growth, and the foramen rotundum and foramen ovale, through which pass respectively the superior and inferior maxillary nerves, were just on the border of the affected area.

ABSTRACT OF APÁTHY'S VIEWS ON THE STRUCTURE OF THE NERVOUS SYSTEM.

This was the title of a paper read, on invitation, by Thos. H. Montgomery, Jr., Ph.D. (Berlin) of the Wistar Institute of Anatomy and Biology.

He said that the structure of the axis-cylinder process has been the object of much discussion, and an equally mooted point is the question as to direct connections between the processes of nerve cells. It is here intended, after a brief historical introduction, to present, without criticism, the results contained in a recent paper by Stefan Apáthy: *"Das leitende Element des Nervensystems und seine topographischen Beziehungen zu den Zellen,"* which appeared in the *Mittheil. d. zool. Station Neapel*, vol. xii, 1897.

The protoplasm (cytoplasm) of the ganglion cell is acknowledged to consist of a denser and a more fluid substance; but the various observers have proposed most divergent views as to the arrangement of these two constituents. Thus Leydig concludes that the denser substance, his spongioplasm, is arranged in the form of an irregular, spongy network in the more fluid hyaloplasm. Hans and Max Schultze, with perhaps the majority of authors, consider the denser portion to be arranged in the form of fibrils. Flemming, that the denser substance, his mitom, occurs in the form of short and isolated fibrils in the fluid paramitom. Bütschli considers the structure of the cytoplasm to be alveolar, and other authors, to consist of granula. Rohde stands alone in assuming the denser substance of the ganglion cell to be produced entirely by strands of neuroglia fibres, which penetrate into the cell body to form a component part of the same.

The structure of the axis-cylinder has, likewise, been most variously described; but we will not take the space here to present more than a few of the more representative of these views. The prevalent idea, founded particularly by Max Schultze, is that it consists of a bundle of primitive nerve fibrils imbedded in a homogeneous matrix; these fibrils entering the cell body, and according to some of the observers, encircling the nucleus. Leydig holds that the hyaloplasm is " *die eigentliche Nervenmaterie* " (the real nervous material), and alone forms the core of the axis cylinder, which is enveloped by a sheath of spongioplasm (not to be confused with the sheath of Schwann, formed by external neuroglia fibres). In a recent study on the elements of the central nervous system of the *Nemertini* (a group of worms), I reached essentially the same conclusions; and indeed this view has been adopted by many investigators of the invertebrates. Nansen in a brilliant paper modifies the view of Leydig, describing the axis cylinder as consisting of a bundle of nerve primitive tubules, each such tubule formed of a hyaloplasmic core and a spongioplasmic sheath. Bütschli holds that the primitive fibrils are nothing but much elongated rows of alveoles.

As to anastomoses or direct connection between the processes of ganglion cells, it may be said to be the most generally accepted modern view that such do not exist.

Apáthy has studied principally the nervous system of the leech *(Hirudo)* and of the earth worm *(Lumbricus)*: but reached essentially the same conclusions for these cells in other *Hirudinea* and *Mollusca*, and in vertebrates, in *Lophius*, *Triton*, the rabbit, and the ox. He maintains that his own methods of preparation, which are the results of years of careful experimentation, are the only ones adequate for the clear differentiation of his neurofibrils. These are (1) a gold impregnation method (after fixation); (2) a methylene blue staining method, and (3) staining with a certain hematein solution. These methods are explained fully in his recent paper (with the exception of the previously-described methylene blue method), and though the *modus operandi* of each is complex, and necessitates especial adaptation for each object to be studied, it furnishes, nevertheless, very clear and beautiful preparations.

Apáthy distinguishes between nerve and ganglion cell as follows: The nerve cell is the producer of the neurofibrils, and hence the producer of that which conducts; while the ganglion cell produces that (force) which is to be conducted; " a division of labor, which has differentiated the neuroganglion cells, with both kinds of functions, into these two cell forms which differ histologically and histogenetically."

According to him there are various kinds of connections between ganglion cells serving to place them in direct and indirect conjunction, and such anatomical connections are histogenetically referable to intercellular bridges. (1) Two cells send a process (either dendritic or axonic) into the same nerve; or (2) the processes of several cells join to form one, or one cell is apposed to another; or (3) a process of one cell is joined with the cell process of another, or a number of such intercellular bridges are present, or (4) two cells are united by their collateral or terminal branches; or lastly (5), and this is "the principal mode and means of the conducting connection," the processes (axis cylinders) of two cells pass over, by continued ramification, into an anastomosing lattice-work. All these types of gangion cell unions were demonstrated by his preparations.

He finds that the neurofibrils are produced by the nerve cells, and in the leech also by the neuroglia cells, so that in this animal, at least, neuroglia cells must be regarded as nervous and not as simple connective tissue elements. Such neuroglia cells may produce both neurofibrils and neuroglia fibrils, or only one of these kinds of fibrils. These two kinds of fibrils are easily distinguished from one another and from connective tissue fibrils by his staining methods. Each neurofibril consists proximally of a bundle of elementary fibrils; but in the course of ramification of the former, bundles of these elementary fibrils are given off, so that at the distal end of a neurofibril only a single elementary fibril remains. The course of the neurofibrils is undulatory. Varicosities of nerve fibres are artefacts.

Now the most important result of Apâthy's studies is that a neurofibril, arising in some particular nerve cell, passes out of one of the processes of the latter, and in its further course may transverse several ganglion cells, and passing out of these again, finally terminate in or around a muscle or sense cell. In the leech the ganglion cells are small and close together, and these results were derived from a study of thick sections, in which only the neurofibrils were deeply stained. From the importance of this conclusion it is necessary to consider more in detail the mode of distribution of neurofibrils in ganglion cells.

In the leech *(Hirudo)*, the object most fully studied, he found the body of the ganglion cell to consist of the following layers, enumerating from the outside: (1) the outer glia zone; (2) the inner glia zone; (3) the outer alveolar zone; (4) the outer so-called "chromatin" zone, the granules of which are chemically comparable to chromophilic granules; (5) the inner alveolar zone; (6) the inner "chromatin" zone, connected with the outer corresponding zone by radial bridges; and (7) the perinuclear zone, in which is a corpuscle comparable to a centrosome. The

"*Stammfortsatz*" of the cell does not correspond alone to the axis-cylinder process of the vertebrate ganglion cell, but to axis-cylinder, plus dendritic processes (these cells are unipolar); this process consists, apart from the contained neurofibrils, of a dense, almost homogeneous substance.

According to the mode of distribution of neurofibrils in ganglion cells, Apáthy distinguishes two types of cells: (G) that of the larger, and (K) that of the smaller cells. In the first type the neurofibrils form a lattice work within the outer "chromatin" zone of the cell, and are irregularly grouped in the whole diameter of the axis cylinder; they come out of this process, coursing mainly meridionally, and after continued ramifications and anastomoses reach the apex of the cell, and then, on the opposite surface of the "chromatin" zone of the latter, collecting together again, pass out into the cell process. "The cell process contains accordingly cellulipetal as well as cellulifugal neurofibrils, and in the cell body the cellulipetal neurofibril passes directly over into the cellulifugal." This first type of cells contains no inner "chromatin" zone. In the second type of cells the neurofibrils are grouped into two zones, concentric hollow spheres of anastomosing fibrils, these two zones being connected by radial neurofibrils; (1) the perinuclear lattice work, which lies in the cell body at the boundary of the perinuclear and inner alveolar zone; and (2) the perisomal lattice work, which lies in the outer "chromatin" zone of the cell.

In this second type of cells, then, the cellulipetal fibrils pass from the cell process into the perisomal lattice work, composing the latter, and from there pass radially to the inner, perinuclear lattice work, and at the distal pole of the latter converge to form a single, thick, cellulifugal neurofibril. "The thick, axial primitive fibril of the cell process accordingly represents the cellulifugal, and the more peripheral, thinner primitive fibrils the cellulipetal portion of the conduit, and the whole ganglion cell of type K is most probably motor." That is, the thicker neurofibrils are motor, the thinner, sensory. "No primitive fibril passes through the ganglion cell without having ramified and taken part in the production of a lattice work within the cell body. And, on the other hand, no entering primitive fibril terminates in any way within the cell body, nor does a departing fibril arise in the ganglion cell." Essentially the same conclusions were reached also for the ganglion cell of *Lumbricus*, and cells of the spinal chord and medulla oblongata of *Lophius*, *Triton* and *Bos*.

In *Lumbricus* the large cells of Leydig are not ganglion cells, though they may be nerve cells.

The terminal neurofibrils, on reaching nerve and muscle cells, enter these cells but do not terminate within them, but leave them again to anastomose around them. In ciliated epithelia the neurofibrils appear not to enter the cells, but to form an intercellular lattice work.

Such are, as briefly as possible, the most striking results of Apáthy's researches. His figures seem to be quite convincing, and more than one colleague, on seeing his preparations, has been won over to his views. The main object of this review has been to make American neurologists acquainted with this important paper, which might not, otherwise, have become so quickly known to them, since it was published in a zoological journal. We should not remain skeptical as to the truth of his results, but rather test their validity by using the microscopic methods recommended by him. For if these results be corroborated, the structure of the nervous system will be placed in an entirely new light, necessitating a complete reversal of most of our present ideas.

DISCUSSION.

Dr. Chas. K. Mills:—This is one of the most important communications ever made to this Society, and while I do not feel competent to discuss the matter from the standpoint presented, I cannot fail to express my thanks to the speaker for its presentation. As has been said, these views are not only reactionary, but revolutionary, and if confirmed, will compel us to recede from the views recently adopted as to the nerve cell as an anatomical unit. Our theories of the neuron must disappear or be largely modified. We must wait for a full confirmation of views so revolutionary.

Dr. Spiller:—Possibly many here present will share the incredulity I experienced when I first heard these statements When I learned, however, that Apáthy had been working on these investigations many years; when I read a letter from one of the most famous histologists in the world confirming his statements; when I heard that his specimens had been examined by many men and had been acknowledged by them to be demonstrative; when I saw the careful manner in which the paper had been prepared; it seemed to me that the subject was too important to be dismissed lightly.

If these views are accepted they will upset our present conceptions. Anastomoses of nerve cells! We are going back to something resembling the old views of Gerlach. It is not easy to believe that neuroglia cells are nerve cells. We know that neuroglia cells and nerve cells have embryologically a common origin, but we have believed that in their full development they are very different structures. Fibrils within the protoplasm of the ganglion cells (in the old sense) have been described by many. A friendly strife has arisen between Lenhossék and Flemming. The former at one time stated that he was unable to find the fibrillary structure in the axis cylinder of the spinal ganglion cell, but this year he has published a careful study on the spinal ganglion cells of man in which he acknowledges the existence of fibrils within the axis cylinder. He has been unable to observe them within the cell body. Flemming has replied to this paper and has stated positively that they are present also within the latter.

Van Gehuchten, at the recent congress in Moscow, read an important paper on the structure of the nerve cell. He says that ganglion cells contain a network on which there is an incrustation of chromophilic substance; that in certain places this incrustation is sufficient to produce the Nissl corpuscles; and that the vacuoles, which have been observed within these corpuscles, are the meshes of the network which have not been filled by chromophilic matter. I do not find, however, any reference to Apáthy neurofibrils in this report.

Some years ago Marinesco advanced the theory that a nerve cell (in the old sense) is only kept in a normal condition by the reception of impulses from the periphery of the body and from the brain. If either source is cut off, the cell suffers. A short time ago I had occasion to express the opinion that the possibility of tertiary degeneration in cerebral hemiplegia had never been irrefutably demonstrated. Soon after I had made this statement, Schaffer's paper, in which changes are described which occurred in the motor cells of the spinal cord in hemiplegia forty-eight days after the beginning of the attack, came into my hands. He believes that the atrophy of hemiplegia is the result of destruction of motor fibres in the pyramidal tract. These views come to us in a new light if we may believe that there is direct continuity of neurons by means of neurofibrils, and not merely a loss of impulse to motor spinal cells.

As another illustration; Marinesco described changes in the cells of the posterior nucleus of the vagus from peripheral lesions of this nerve and concluded, therefore, that this nucleus must be motor. Van Gehuchten states that he has found changes in the acoustic nucleus of the oblongata a short time after section of the eighth nerve. The axis cylinders which pass into this nucleus, *terminate* about its cells. He believes that changes occur in the cell body of the central neuron after lesion of the peripheral neuron. If we dare believe that neurofibrils pass from the first neuron into the cell body of the second, we can readily understand why there should be an alteration of structure in the latter.

Let us look at the subject of the reflexes in the light of Apáthy's discoveries. If it is true that neurofibrils pass from sensory fibres into motor cells, we may be able to better understand the difficult subject of the reflexes. It is not unusual in great exaggeration of the reflexes to obtain contraction of the adductor muscles of one thigh by striking the patellar tendon on the opposite limb. A reflex is not limited to one or even a few muscles. If neurofibrils pass through a number of ganglion cells, we may readily understand how an impulse acts on many cells.

Dare we believe that the many neurofibrils which leave a sensory cell, in contrast to the single one which leaves a motor cell, are indicative of the conveyance of different forms of sensation?

These are only a few thoughts which occur to me. I am seeking light, not stating facts, and am well aware of the danger of theorizing, but time will demonstrate the truth or fallacy of these suggestions.

NEW AESTHESIOMETER.

In the June number of the Bulletin of the Johns Hopkins Hospital, Dr. L. F. Barker describes an ingenious little instrument recently prepared by Professor Von Frey for studying pain and pressure sense. It is an improvement on an apparatus previously described from Von Frey's clinic by Dr. Barker, in which the amount of pressure necessary to bend test hairs of various diameters was employed. The new instrument has the advantage that with a single hair one can obtain a number of different pressure values.

It consists of a long hair pushed through a capillary tube like a thermometer tube; by sliding a sheathing over the tube it may be made to project more or less. According to the length of the projection of the hair is the strength which is necessary to make it bend, and a reading of the scales inscribed upon the tube gives thus some idea of the force used. Dr. Barker quotes a case in evidence of its usefulness, in which ordinary slight stimuli appeared to cause pain. It was supposed that pressure sense was absent. It was easy with this instrument to prove that pressure sense was not abolished, though the level for pain was almost the same as that for touch. The importance for such an observation is obvious for showing the retention of tactile sense in cases where it is obscured by hyperesthesia. MITCHELL.